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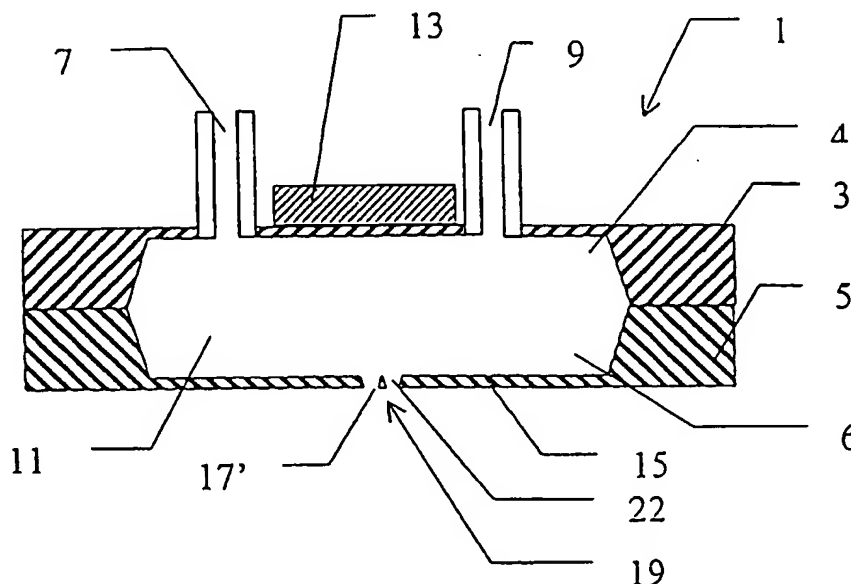
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(54) Title: **DEVICE FOR DISPENSING DROPLETS**



(57) Abstract: Dispensing nozzle (19, 19', 19'') for dispensing drops containing a volume of 1000 nanolitres or less from a reservoir (11) having a dispensing surface (15) wherein said nozzle (19, 19', 19'') comprises a dispensing outlet (21) leading from said reservoir (11) to said dispensing surface wherein said outlet (21) has a plurality of dispensing orifices (17', 17'', 17''') at its end which is furthest away from said reservoir (11).

WO 01/30500 A1

Device for dispensing droplets**Field of the Invention**

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The present invention relates to devices for dispensing small quantities of liquids through nozzles.

Prior Art

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In the field of micro-assaying, pharmaceutical production and other dispensing processes, it is often necessary to supply very small doses or samples of a reagent or substance being tested. Patent application WO97/01085 describes a flow-through sampling cell in which it is possible to dispense individual droplets which each contains a very small volume of fluid. This document teaches a device for dispensing droplets of a sample wherein the device has an etched silicon membrane that has a 60 micro-metre (μm) diameter dispensing orifice. This orifice yielded a drop diameter of 40 μm that corresponds to a drop volume of 34 pico-litres (pl).

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In the fields of micro-assays, pharmaceutical production and the like, there is often a requirement for larger droplets containing sub-microlitre volumes of fluid and attempts have been made to produce such droplets by producing larger diameter dispensing orifices. These attempts have not achieved a satisfactory performance because, when using the reagents typically used in such fields, the increased orifice diameter leads to undesirable leakage through the orifice. This is because the diameter of the enlarged orifice is so big that the surface tension of the fluid acting on the rim of the orifice is insufficient to prevent the fluid leaking out of the orifice.

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Summary of the Invention

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The above problem with the prior art devices for dispensing small droplets is solved by means of a device in accordance with the characterising part of claim 1.

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In particular, in a first embodiment of a device in accordance with the invention, droplets to be dispensed are fed from a reservoir via an outlet duct to a dispensing nozzle provided with a

plurality of dispensing orifices. In this way leakage is prevented while an increased drop size is obtained.

- 5 In a further example of a device in accordance with the invention the perimeter of the rim of the end of the outlet duct nearest to said reservoir is greater than the perimeter of the rim of each dispensing orifice at the exterior end of an outlet duct. This large size of the rim of the outlet duct minimises the backpressure in the outlet duct, while the smaller perimeters of the rims of the dispensing orifices prevents leakage.
- 10 In another example of a device in accordance with the invention the perimeter of the end of an outlet duct nearest to said reservoir is larger than the perimeter of the end of said outlet duct furthest away from said reservoir (e.g. by the outlet duct being formed with a conical or tapered shape) in order to further reduce the backpressure.
- 15 Example of embodiments of the invention will be described below in more detail with reference to the accompanying figures.

Brief Description of the Figures

- 20 Figure 1a) shows a cross-section along line I-I in figure 1b) of a dispensing device with a nozzle in accordance with the prior art;
- Figure 1b) shows a plan view of the device in figure 1a);
- 25 Figure 2a) shows a cross-section along line II-II in figure 2b) of a dispensing device with a nozzle in accordance with a first embodiment of the invention;
- Figure 2b) shows a plan view of the device in figure 2a).
- 30 Figure 3a) shows a cross-section through a second embodiment of a nozzle in accordance with the invention.
- Figure 3b) shows a show a plan view of the embodiment of figure 3a).
- 35 Figure 3c) shows a cross-section through a variation of the second embodiment of a nozzle in accordance with the invention.

Figures 4a) shows a plan cross-sectional view along line IVb-IVb in figure 4b) of a third embodiment of the invention.

5 Figure 4b) shows a cross-section along line IVa-IVa in figure 4a).

Detailed Description of Embodiments Illustrating the Invention

Figure 1a) shows a cross-sectional view of a prior art sampling cell 1 comprising a first
10 structure 3 and a second structure 5 which have been attached together. These two structures 3, 5 are made from, for example, etched silicon. The first structure 3 has a first basin 4 etched in it and the second structure 5 has a second basin 6 etched in it. When the two structures 3, 5 are bonded together these two basins 4, 6 form a reservoir 11 which also acts as a flow channel as fluid that enters the cell 1 via an inlet 7 can flow through reservoir 11 to an outlet
15 9. The cell is provided with a pressure pulse generating piezo-electric disc 13 which can be activated by control means (not shown) to generate a pressure pulse in the reservoir 11. Reservoir 11 has a dispensing orifice 17 (not shown to scale in the figures for the sake of ease of illustration) with a diameter of 60 μm formed in the bottom, dispensing wall 15 of the second basin 6. If the piezo-electric disc 13 is controlled to apply a suitable pressure pulse to
20 the fluid in reservoir 11, a drop of fluid can be ejected through the dispensing orifice 17. Typically, for aqueous solutions, the drop will have a diameter of 40 μm and a volume of 34 pico-litres (pl). The higher the surface tension of the liquid, the greater the resulting drop size.

Figure 1b) shows a plan view from below of sampling cell 1.

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Figure 2a) shows schematically a cross-section through a sampling cell having a first embodiment of a dispensing nozzle in accordance with the invention. Features of this device which are the equivalent of those shown in figure 1 have been given the same reference numerals used in figure 1. The sampling cell of figure 2a) differs from the sampling cell of
30 figure 1 by it being provided with a dispensing nozzle 19 comprising a plurality of outlet ducts 22 which each lead from reservoir 11 to their own dispensing orifice 17'. In the example shown in figures 2a) and 2b) the nozzle 19 is made up of 4 closely spaced dispensing orifices 17'. The maximum size of each of the dispensing orifices 17' is chosen so that each orifice 17' is sufficiently small so as to prevent undesirable leakage of the fluid from the
35 reservoir 11. At the same time, the minimum size of each orifice 17' is chosen so that each orifice 17' is sufficiently large so that the pressure at which fluid breaks away from the rim of

each orifice 17' is not greater than that which can be provided by the piezo-electric pressure pulse generator 13. Preferably the size of each orifice 17' is adapted so that the pressure is the same for each orifice 17' so that fluid is dispensed substantially simultaneously from all the orifices 17'. This can be achieved by having substantially identically shaped orifices or by
5 having orifices with substantially the same perimeter length. The spacing between the orifices is chosen such that when fluid is dispensed through the dispensing orifices 17' the distance between the individual droplets emerging from each of the orifices 17' is sufficiently small so that the droplets can come into contact with each other and combine to form one larger drop. Preferably, the distance between each orifice 17' is less than the maximum width of an orifice
10 and should be as small as possible, due regard being paid to the mechanical strength of the material between the orifices. The number and sizes of the orifices 17' are chosen so that when the droplets combine they form a drop of the desired volume. Preferably the circumference or perimeter of each orifice should be between 3 and 300 micrometer which, in the case of circular orifices, corresponds to a diameter of approximately 1-100 micrometers.

15 As can be seen in figure 2a), in a preferred embodiment of the invention, the diameter (and consequently the perimeter of the rim) of each orifices 17' at the inner surface of bottom wall 15 is greater than its diameter at the outer surface of bottom wall 15 in order to reduce the pressure drop through the bottom wall 15. This is preferably achieved by tapering each outlet
20 duct 22.

Figure 3a) shows a cross-section through a second embodiment of a nozzle in accordance with the invention. Figure 3b) shows a plan view of this embodiment. The figure is not drawn to scale. The scale in this view has been enlarged in comparison to that in the previous figures
25 in order to improve the clarity of the illustration. In this embodiment nozzle 19' comprises a dispensing outlet 21 which passes through the dispensing wall 15. Dispensing outlet 21 is formed from an outlet duct 22, the outer end of which is covered by a front screen 23 which is formed in the outer surface of bottom wall 15. Preferably, outlet duct 22 tapers from its innermost end to its outer end as shown by dotted lines in figure 3a). Front screen 23 consists
30 of, for example, a fine mesh net 25 with a plurality of dispensing orifices 17''. The orifices 17'' can be produced in front screen 23 before being attached to bottom wall 15 or they can be produced afterwards. The surface area of each orifice 17'' is less than the surface area of the inner end of the duct 22 of outlet 21. In order to reduce the back pressure through front screen 23, the front screen 23 should preferably be made as thin as practical. As shown in
35 figure 3b) some of the orifices 17'' at the edge of the front screen 23 have perimeters which are considerably smaller than the perimeters of the orifices 17'' in the middle of the front

screen 23. The backpressure across the smaller orifices 17'' will be considerably greater than that across the larger orifices and therefore normally the smaller orifices will not permit any fluid to pass through them and will not contribute to forming larger droplets. If desired these orifices could be blocked to avoid them collecting dead volumes of fluid, which could
5 contaminate future fluids passing through the outlet duct. While front screen 23 can be made in situ out of the material of bottom wall 15, it is also conceivable that it can be produced separately and attached by any suitable means to bottom wall 15 as shown in figure 3c). When water is used as a solvent, it is conceivable to cover the exterior surfaces of bottom,
10 dispensing wall 15 with a hydrophobic layer or to treat the exterior surface to form a hydrophobic layer as shown by the thick line 24, in order to prevent the formation of satellite drops and to prevent fluid spreading out sideways from the nozzle. This solvent repelling layer 24 is shown covering the entire exterior surface of wall 15 but it is conceivable to only cover the part of wall 15 nearest to the nozzle 19' in order to obtain the desired effect. Naturally when other solvents are used the solvent repelling layer 24 could be adapted to
15 repel the actual solvent being used.

Figures 4a) shows a plan cross-sectional view of a third embodiment of the invention. The view is not to scale. In this embodiment nozzle 19'' comprises a plurality of dispensing orifices 17''' in the shape of circle sectors arranged in concentric rings around a central
20 circular orifice 17'''. Preferably the dimensions of the orifices are chosen so that they all have substantially the same backpressure. As can be seen from the cross-section shown in figure 4b) the diameter of outlet 21 leading through the dispensing bottom wall 15 is greater than the diameter of nozzle 19'' in order to reduce the backpressure through the outlet.

25 Preferably outlet ducts should be tapered from a large perimeter at the reservoir end to a smaller perimeter at the dispensing orifice end in order to keep the back pressure in the duct as low as possible. Where possible the outlet ducts should meet the orifices at angle which prevents the forming of dead volumes which otherwise can retain small volumes of fluid, which can be difficult to rinse away, and which can contaminate further fluids used in the
30 device.

Claims

1. Dispensing device comprising a dispensing nozzle (19, 19', 19'') for dispensing drops
5 containing a volume of liquid of 1000 nano-litres or less from a reservoir (11) having a
dispensing surface (15) wherein said nozzle (19, 19', 19'') comprises a dispensing outlet (21)
leading from said reservoir (11) to said dispensing surface (15) characterised in that said
outlet (21) has a plurality of dispensing orifices (17', 17'', 17''') at its end which is furthest
away from said reservoir (11).
10
2. Dispensing device in accordance with claim 1 characterised in that the perimeter of the
rim of each dispensing orifice (17', 17'', 17''') is less than the perimeter of the rim of the end
of the outlet (21) nearest to said reservoir (11).
- 15 3. Dispensing device in accordance with any of the previous claims characterised in that
the perimeter of the end of said outlet (21) nearest to said reservoir (11) is larger than the
perimeter of the end of said outlet (21) furthest away from said reservoir (11).
4. Dispensing device in accordance with any of the previous claims characterised in that
20 said outlet (21) comprises a single duct (22).
5. Dispensing device in accordance with any of claims 1-3 characterised in that said
outlet (21) comprises a plurality of ducts (22).
- 25 6. Dispensing device in accordance with any of the previous claims characterised in that
the total length of the perimeters of each dispensing orifice (17', 17'', 17''') is less than the
total length of the perimeter or perimeters of the end of said duct or ducts (22) which is
closest to said reservoir (11)
- 30 7. Dispensing device in accordance with any of the previous claims characterised in that
said at least one of said dispensing orifices (17') has a substantially circular cross-section.
8. Dispensing device in accordance with any of claims 1-6 characterised in that at least
one of said dispensing orifices (17''') has a cross-section in the shape of a sector of a circle.

9. Dispensing device in accordance with any of claims 1-5 characterised in that at least one of said dispensing orifices (17'') has a cross-section of square or rectangular or polygonal shape.
- 5 10. Dispensing device in accordance with any of the previous claims characterised in that said outlet (21) tapers from the reservoir (11) to said dispensing surface (15).
11. Dispensing device in accordance with any of the previous claims characterised in that a portion of said dispensing surface (15) is provided with a solvent repelling layer (24).

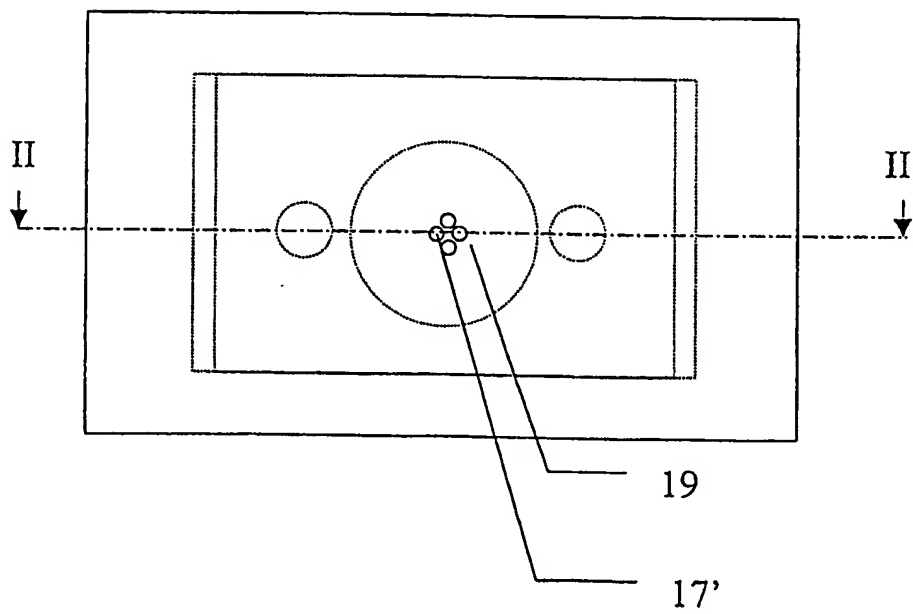
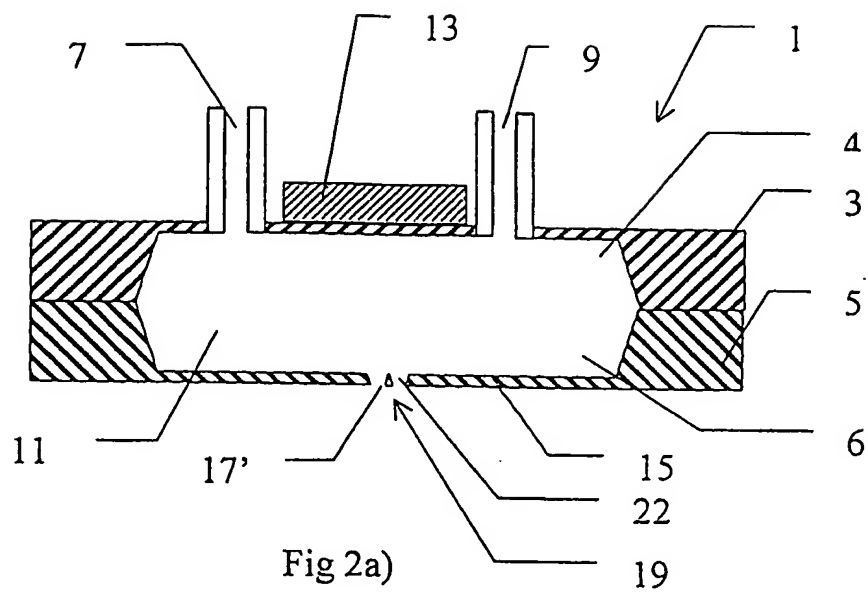


Fig. 2b)

Fig. 3a)

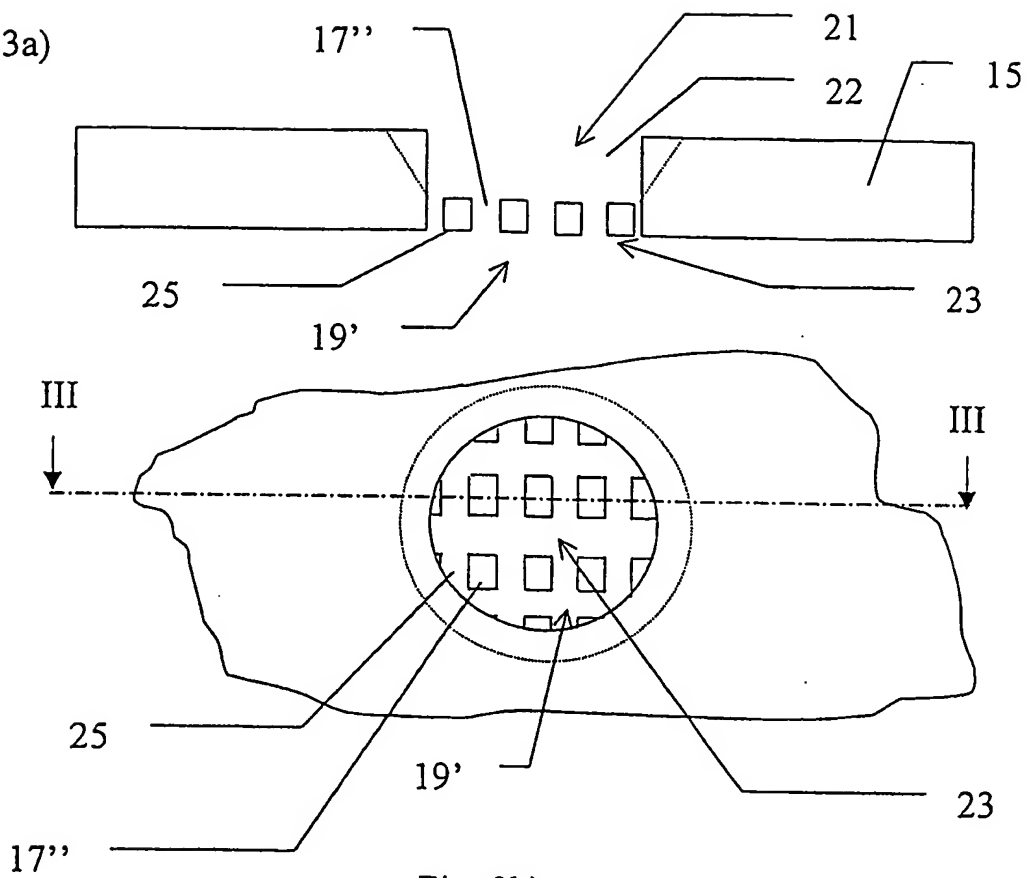


Fig. 3b)

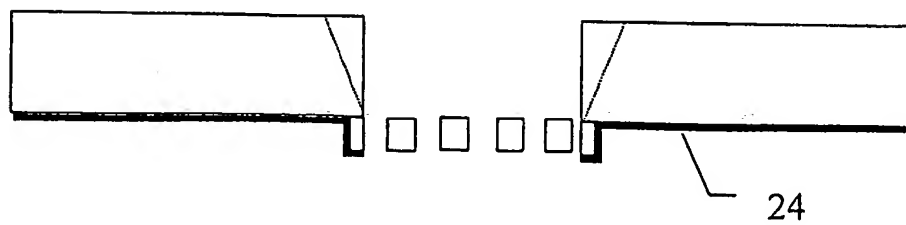
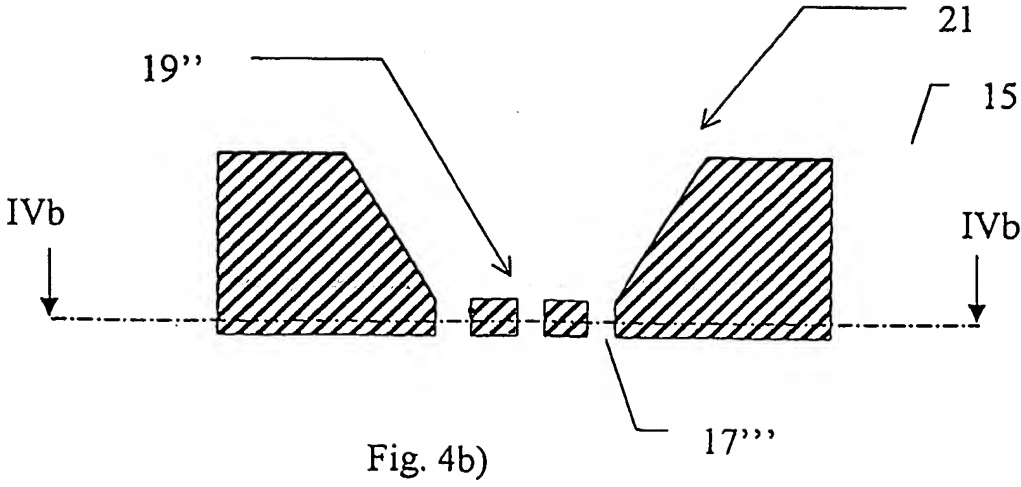
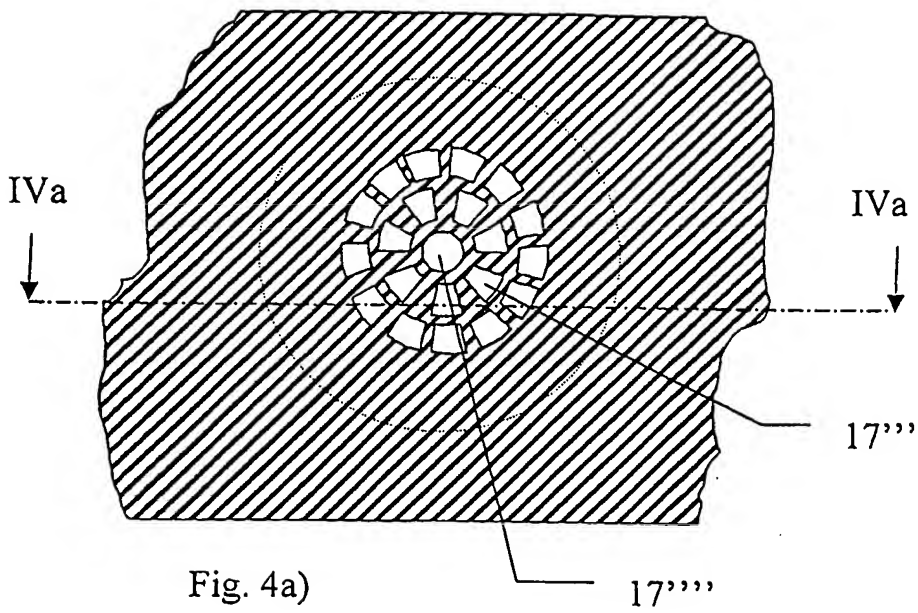


Fig. 3c)



INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 00/02097

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: B01L 3/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: B01L, G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 9936176 A1 (CENTRAL RESEARCH LABORATORIES LTD.), 22 July 1999 (22.07.99), page 5, line 19 - line 22, figures 1-2 --	1-10
X	WO 9701085 A1 (PHARMACIA AB), 9 January 1997 (09.01.97), page 8, line 26 - line 28	11
A	abstract --	1-10
A	WO 9715394 A1 (SMITHKLINE BEECHAM CORPORATION), 1 May 1997 (01.05.97), figures 1-2, abstract -----	1-11



Further documents are listed in the continuation of Box C.



See patent family annex.

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INTERNATIONAL SEARCH REPORT
Information on patent family members

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Patent document cited in search report			Publication date	Patent family member(s)		Publication date
WO	9936176	A1	22/07/99	AU	2174499 A	02/08/99
				AU	6844798 A	22/10/98
				EP	0973380 A	26/01/00
				EP	1054734 A	29/11/00
				GB	9800933 D	00/00/00
WO	9701085	A1	09/01/97	AU	6246396 A	22/01/97
				CA	2224278 A	09/01/97
				EP	0835435 A	15/04/98
				JP	11508360 T	21/07/99
				SE	9502251 D	00/00/00
WO	9715394	A1	01/05/97	EP	0862497 A	09/09/98
				GB	9521775 D	00/00/00
				JP	2000500567 T	18/01/00